

as our methods become more refined. Finally, the development of rather more specific operational concepts in the field of depression commends itself to the investigator, who may then have the opportunity of going beyond the mere assessment of the therapeutic value of the given agent.

SUMMARY

Although antidepressant drugs have made an extraordinary impact on the treatment of depressive illnesses, our present level of knowledge of the mechanism of action of these agents is still most incomplete.

Desmethylinipramine, the monomethyl analogue of imipramine, has been shown to have an exceedingly rapid onset of action in laboratory animals. Preliminary findings with its use in depressed patients are presented.

As an antidepressant drug, its efficacy is in the range of that of imipramine itself. Side effects, too, were similar.

Rapid onset of action was not consistently noted in this study.

Desmethylinipramine seems worthy of more extensive investigation, particularly with a view to better definition of the general fields and concepts of depression, and more intensive study of the early signs of improvement.

Thanks are due Geigy Pharmaceuticals for supplying us with generous amounts of desmethylinipramine (G-35020).

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Electrophysiological Localization and Identification of Subcortical Structures as an Aid to Stereotaxic Surgery:

A Preliminary Report

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FUNCTIONAL exploration of subcortical structures in man is routinely performed during stereotaxic surgical operations. Its importance is emphasized by the fact that none of the periventricular structures usually taken as a reference has a constant anatomical relationship to the thalamic nuclei.^{2, 4} Therefore, unpredictable individual anatomical variations could be responsible for topographical errors in the placement of the electrode; hence the need to verify its actual position after placement.

Exclusive and specific identification of subcortical structures in man has so far not been obtained by any of the functional exploration methods. Depth recording has not aided in the recognition of particular rhythms of the electrical activity from the various structures.⁶ The actual methods of recording were such that it was not possible to differ-

entiate clearly between electrical activity arising from white matter and from grey matter.¹

Stimulation techniques, although providing some useful corrections, are still approximate, because most of the structures which are stimulated, except the nucleus ventralis posterior, give various responses the specificity of which is difficult to establish. Similarly, contralateral motor responses obtained from stimulation near the internal capsule, with the same parameters, are variable from one patient to another, owing to unknown tissue resistance and unpredictable current spread. Even then, enhancement of tremor in parkinsonian patients, by means of artificial stimulation, is not specific to a particular thalamic nucleus, since the diffuse reticular system may be simultaneously stimulated.

However, identification of subcortical structures, and particularly differentiation between white matter and subcortical grey matter, has been accomplished in experimental electrophysiological studies on animals. It appeared important to attempt the application of the techniques to human neurophysiological investigations.

An electrophysiological stereotaxic recording method was then devised and successfully applied

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to the human.* This technique utilizes bipolar, concentric, metallic electrodes of different types with a point sufficiently fine (less than 50 microns) to record rapid activity of cell units. This activity is amplified and monitored on a cathode-ray oscilloscope and also broadcast through a loudspeaker.

By this method of recording rapid activities arising from cell units, it was possible to differentiate clearly between electrical activity from the white matter and that recorded from the grey matter. Reconstruction of the patient's cortical folds was then designated on a schematic map on the basis of this electrophysiological information. This technique also permitted the definition, within a fraction of a millimetre, of the anterior and posterior limits of the thalamus, the width of the internal capsule and the length of the globus pallidus.

Within the thalamus, some nuclei were identified by the difference in the background electrical activity. The nucleus ventralis posterior and its subdivisions, ventralis posterior lateralis (VPL) and ventralis posterior medialis (VPM), were recognized also by recording evoked potentials induced by tactile stimulation of the corresponding surface of the body. Similarly, the nucleus ventralis lateralis—the target structure—was precisely defined between the nucleus ventralis posterior behind and the internal capsule in front. At its anterior border, the nucleus reticularis (*zone grillagée d'Arnold*) was also recognized over a distance of 1.5 mm.

This method of delimiting the thalamic nuclei is anatomically precise (and overcomes the inaccuracy inevitably encountered when one works from an atlas based on the average of numerous dissections).

In the course of these investigations, rhythmic activity at the same frequency as the tremor was

recorded in the thalamus, particularly from the nucleus ventralis posterior. We have stressed elsewhere⁵ the importance of these rhythmic cells, the discovery of which would eventually contribute to the understanding of the mechanisms of parkinsonian tremor. These observations on the thalamus of man correlate with the finding, by Cordeau and co-workers,³ of rhythmic potentials synchronous with tremor in the sensorimotor cortex of monkeys. As these rhythmic potentials begin and end with the tremor, they would appear to be evoked by excitation of the somatic sensory receptors from the shaking limb. Even if these rhythmic potentials are not directly involved in the origin of tremor, they could constitute a feedback source of abnormal impulses which facilitates the oscillating circuit responsible for the tremor. Other cells showing rhythmic activity were encountered in the thalamus, particularly in the pulvinar, but their frequency had no apparent relationship to the frequency of tremor.

SUMMARY

Stereotaxic electrical recording is a new method for the functional exploration of the subcortical structures in man. It provides an accuracy of localization of thalamic nuclei which cannot be obtained by other methods so far employed. This acquisition for neurosurgery and human neurophysiology can contribute to better knowledge of the physiology and physiopathology of the extrapyramidal system.

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*Preliminary results were presented at the Symposium on Physiopathology and Neurosurgery of the Extrapyramidal System, Madrid, November 1961.

PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

AN INCIDENT IN THE LIFE OF HARVEY

Harvey is reputed to have been very quick-tempered, and it must have been terribly trying to him to be detained in a wretched, dirty lazaretto for two weeks, writing frantic letters every day to Lord Fielding imploring the intervention of the government, and of the College at Venice. He slept at first in the open field, as they wished to put him in the lazaretto where he might, as he says, have taken the infection. The phraseology and spelling of the letters are interesting, e.g.—“I am a little jealous of them, and to take anny beds now of ther sending, for since ther manners and cruelty hath beene soe shamefull to me, and they have soe little reason for what they have done, it would be like the rest of ther proceedings yf they sent me

an infected bed to make ther conjectures and suspicions prove true; therfor I choose to ley still to be redeemed by your Excellency oute of this innocent straw. Yesterday likewise the patron that owed the house wheare I first took my straw bed (a little poore garden howse full of lumber, durt and knatts, without window or dore, open to the high way att midnight) was to offer me that agayne, because I had chosen that to shun the infamy of this lazeret and the suspicion I had that sum infected person had lately bene heare, and from which they forced me with terror of muskets, I write this to shew your Eccellency that all they doe haere upon your stirring is butt formal to salve their own errors.”—Sir William Osler: *Men and Books*, *Canad. Med. Ass. J.*, 2: 246, 1912.